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**ADOLESCENT KNEE PAIN AND PATELLAR DISLOCATIONS ARE  
ASSOCIATED WITH PATELLO-FEMORAL OSTEOARTHRITIS IN  
ADULTHOOD: A CASE CONTROL STUDY**

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## **1. Introduction**

Patellofemoral Osteoarthritis (PFOA) is frequently identified as a disease of middle to old age, with Noble and Hambleton reporting PFOA in 79% of cadavers aged  $\geq 65$  years [1], and radiological evidence of isolated PFOA in 14% of women, and 15% of men, greater than 60 years of age [2].

The term adolescent Anterior Knee Pain (adolescent AKP) syndrome represents a constellation of symptoms, and has traditionally been thought of as a benign condition. Studies from 1985 have explored relationships within the syndrome [3], with prevalence estimated between 33% [4] and 91% [5]. Although throughout this period it was considered self-limiting, more recent reports have begun to show a link between adolescent AKP and PFOA. However, a systematic review in 2010 concluded that currently 'there is a lack of sound evidence from epidemiological studies on the association between AKP in younger adults and subsequent PFOA' [6].

Furthermore, there is little available data on whether a history of patellar dislocation is a risk factor for the subsequent development of PFOA, although older studies dating back to 1952 have remarked upon indirect associations [8].

The aim of this study is to determine the relative prevalence of adolescent AKP and previous patellar dislocations in patients with severe, symptomatic isolated PFOA and in a control group of patients with severe medial compartment knee OA. These comparative relationships will then be analysed and evaluated using a multivariate model.

## **2. Methods**

### **2.1 Study design**

A case-control study was performed using our knee arthroplasty database to identify 190 patients who had undergone a patellofemoral arthroplasty (study group), and a control group of 445 patients who had had a medial unicompartmental knee arthroplasty, both surveyed between 4- and 8-years post-operatively.

The inclusion criteria for the patellofemoral arthroplasty group were the presence of severely symptomatic and radiologically confirmed PFOA, and the absence of radiological signs of OA in the medial or lateral tibiofemoral compartments. This is represented by a clearly defined cohort of patients with severe symptomatic isolated PFOA requiring patellofemoral joint arthroplasty as determined by their treating surgeon. By the same measure, the criteria for the unicompartmental control group meant that the patients would have minimal, if any, PFOA at the time of the operation, with severely symptomatic and radiologically confirmed medial compartment tibiofemoral OA requiring arthroplasty. Any patient on the database who had recently taken part in another research study was excluded to prevent excessive participation burden. This left 635 cases and controls remaining for the study. Only severe

cases of arthritis are included in the analysis. This does not imply that mild arthritides have no associations with a degree of adolescent AKP or patellar dislocation, but as this inclusion criterion was easily and clearly definable, specificity of the population samples increased.

Once identified, each of these patients was sent a postal questionnaire asking them about the symptoms and interventions they had received prior to arthroplasty surgery (see Appendix). A description of previous surgery was requested as a potential confounder in later statistical analysis, as many studies have shown a potential link between types of surgery and development of PFOA [7, 9, 10].

Cases were 1:1 frequency-matched by gender - control cases were individually removed until the gender proportions of each group were equal. To maintain comparability, any discrepancies in mean age between groups were minimised. No patients in the case population were deleted in order to perform the matching as any alterations in the case sample would consequently cause a misrepresentation of the diseased population, and would have affected the generalisability of the results of the study. In addition, blinding occurred throughout; all the data from the questionnaire was temporarily hidden from view during selection.

## 2.2 Statistical analysis

Descriptive demographic data on the questionnaire responses are given as percentages. Incomplete or unclear answers from the questionnaires were treated as missing data points. Adolescent AKP was defined as age 18 years and under and was analysed as a dichotomous variable. The presence of symptomatic patellar instability was defined as two or more positive answers to the questions regarding patellar instability whilst walking, using stairs and whilst playing sports. This dichotomization allowed for more effective comparison to the categorized dislocation variable, as well as better applicability to the multivariate statistical analysis being performed.

Initially, a multivariate correlation was performed including all data from the questionnaire. From this, particular relationships were confirmed for further analysis, and the extent of the effects of confounders could be evaluated.

Binary logistic regression was then used to compare the disease state (PFOA or medial compartment OA - the dependent variables) with the set of independent variables under analysis (patient reported adolescent AKP, history of dislocation, instability and previous surgery) to produce adjusted odds ratio (OR) values (Table 1). The latter two independent variables were added to the model due to their higher levels of correlation with disease, to test robustness of the data and account for any confounders. 95% confidence intervals (CIs) and *p* values were calculated for this multivariate model. A *p* value of <0.05 was considered statistically significant.

Additionally, further comparative sub-analysis in the median age of 1<sup>st</sup> dislocation was performed, as well as an observation of differences between the ages of onset of PFOA between those with and without a history of

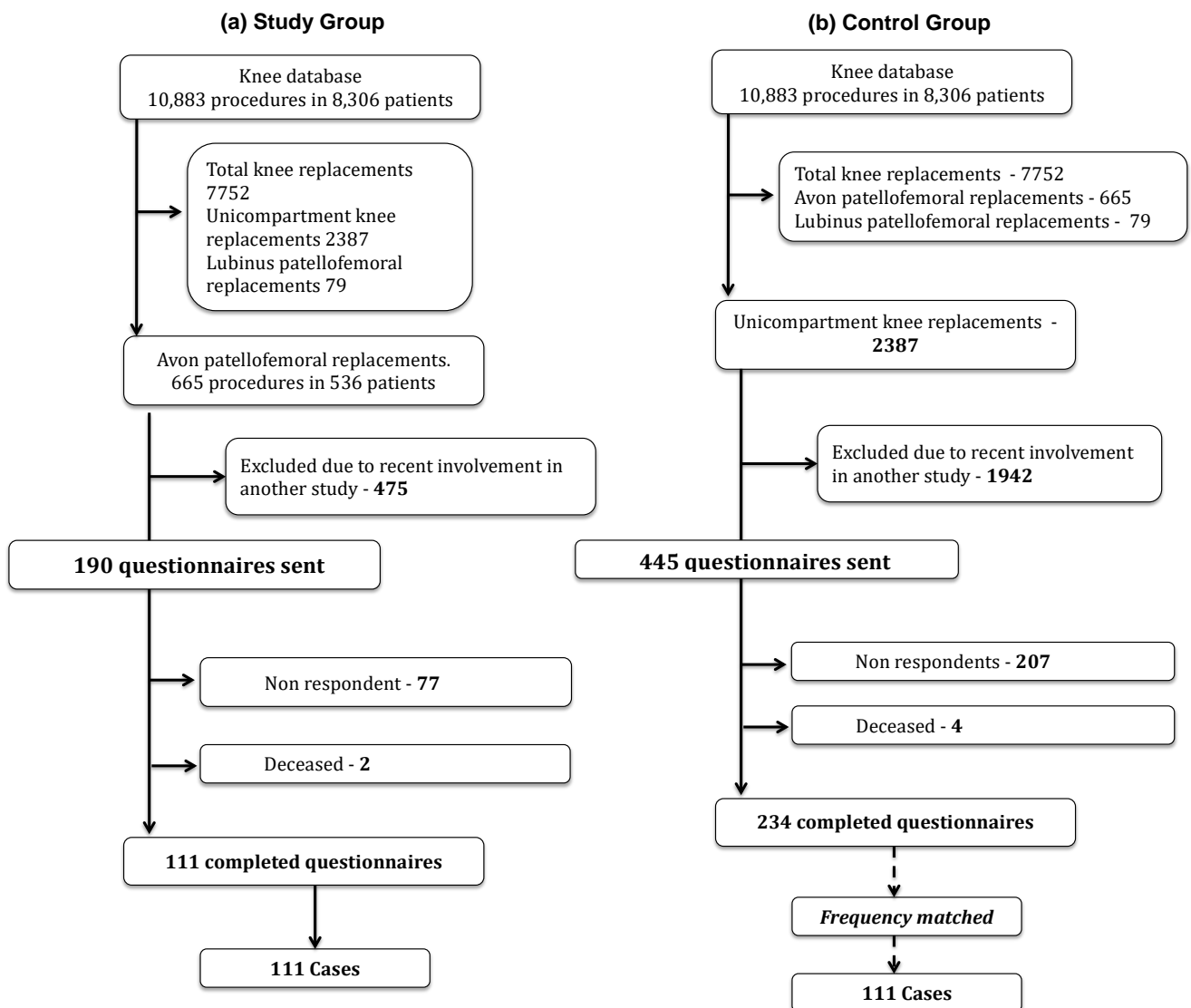
patellar dislocation. The data was identified as non-parametric using a Shapiro-Wilk normality test, therefore median figures and boxplot graphical displays were used.

### **3. Results**

Of the 190 PFOA cases, 111 (58%) were available to take part in the study (see Fig. 1), with a mean age of 60, and a range from 29-89 years. Of these, 77% were female, 23% were male, and 51% were left-sided.

In the control group, a response rate of 53% was recorded, with 234 completed questionnaires returned. After matching, the mean age of the controls was 68 years, with a range from 52-94. 77% were female, 23% male, and 53% left-sided. Before matching, the mean age was 74 and a range of 52-94 was recorded.

**Fig. 1** Flow diagrams summarizing the process for selection of participants in the study group (a) and the control group (b)



**Table 1 – Multivariate binary logistic regression – Adjusted ORs**

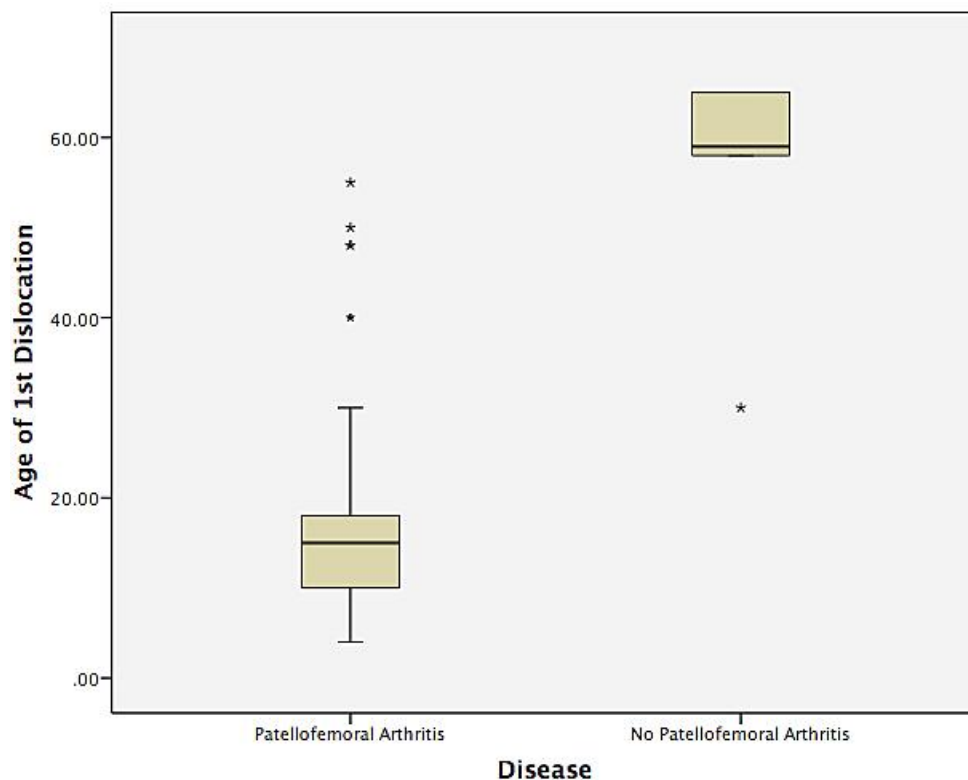
<b>Risk Factor</b>	<b>Unadjusted odds ratio (95% CIs)</b>	<b>Adjusted odds ratio (95% CIs)</b>	<b>p value</b>
<b>Previous Dislocation</b>	8.8 (3.88-19.82)	3.2 (1.25-8.18)	0.016
<b>Adolescent AKP</b>	20.2 (4.69-86.91)	7.5 (1.51-36.94)	0.014
<b>Previous Surgery</b>	6.2 (3.34-11.67)	3.5 (1.75-7.14)	<0.001
<b>Patient-reported instability</b>	5.83 (3.00-11.28)	3.5 (1.62-7.42)	0.001

Unadjusted OR analysis showed that patient reported previous dislocation was significantly associated with PFOA (OR, 8.8; 95% CIs 3.88-19.82) (Table 1).

PFOA was also associated with patient reported adolescent AKP (OR, 20.2; 95% CIs 4.69-86.91).

The multivariate binary regression confirmed that statistically significant associations are present between patient reported adolescent AKP and PFOA (OR, 7.5; 95% CIs 1.51-36.94), as well as patient reported previous dislocation and PFOA (OR, 3.2; 95% CIs 1.25-8.18). Significant values for patient reported instability were also observed (OR, 3.5; 95% CIs 1.62-7.42). Patient reported previous surgery was confirmed as a noteworthy confounder, with an adjusted OR of 3.5 (95% CIs 1.75-7.14).

In those individuals who reported dislocations, the median age of 1<sup>st</sup> dislocation was 15 (range 4 to 55) for the PFOA cases compared to a median age of 59 (range 30 to 65) in the controls in whom this had occurred. This is displayed in Fig. 2. It should be noted that the sample size in the control group was small in this analysis, due to the low rate of patella dislocation in this group (6 cases compared to 42 cases in the PFOA group). Additionally, in the patellar dislocation group, the median age of onset of severe PFOA (i.e. the age at the time of arthroplasty) was 58.2 years, compared to 60.3 years in those who hadn't suffered dislocations.



**Fig. 2** Differences in age of 1<sup>st</sup> dislocation between PFOA cases and unicompartmental arthritis controls (labelled as 'No Patellofemoral Arthritis'). The box length represents the 25<sup>th</sup> to 75<sup>th</sup> percentiles, with the median denoted by the line in the box. The whiskers represent the range, and outliers are marked with an asterisk.

#### **4. Discussion**

Based on our data, if an individual experiences AKP under the age of 18 years, they are approximately 7.5 times more likely to develop severe, symptomatic PFOA later in life. This adds significant weight and evidence to the theory that adolescent AKP is not solely a benign, self-limiting condition.

Whilst studies have shown some evidence of a link between anterior knee pain and development of PFOA, a clear causal relationship has not been established. Reasons vary from small sample populations and follow-up rates [11] to an absence of control groups at the time of recruitment [4]. In the studies that have investigated this, it has been as a secondary outcome or association rather than as the primary outcome or association in the study design. Studies to date have also failed to define what they consider to be PFOA.

Utting et al. used a comparable method to ours to demonstrate evidence of a relationship between AKP and PFOA, with patients who underwent isolated patellofemoral replacement recalling knee pain lasting for an average of 6.4 years longer than those in the medial unicompartmental arthroplasty group [12]. Whilst similar data collection techniques to our study were employed, no matching was performed and basic comparison tests were used, without the use of a logistic regression to take into account the other variables in the study.

Despite the most rigorous search for a specific diagnosis, many adolescent patients are referred to as simply having the idiopathic AKP described in this study, often classed as chondromalacia patella [13]. Whilst it is often accepted that biomechanical factors play at least some role in the disease process and explain the pain experienced [14], further work is required to describe the underlying pathological mechanisms.

Anatomical variations causing biomechanical aberrations such as patella alta and trochlear dysplasia have been implicated as potential causative factors in the development of PFOA [15]. Malalignment and joint laxity may also explain differences between the groups in our study. Although both have been shown to predate osteoarthritic changes in the knee [16, 17], there is no evidence at present that either directly causes PFOA over other forms of arthritis, such as unicompartmental tibiofemoral OA.

Nimon et al. followed up patients with AKP for 14-20 years [11]. They noted that only 22% were pain free at final follow up, and no patient went on to develop signs of structural disease. In contrast, a separate study by Hvid et al. observed approximately 68% of patients with chondromalacia patella had developed biomechanical structural abnormalities [18]. However, the latter study's conclusions must be approached with caution; individuals were only recorded with a 'significant clinical syndrome', a criticism that has been noted by other authors [6].

Unicompartmental arthroplasty patients were chosen as the control group due to the presence of some osteoarthritis, compensating for recall bias based on pain and awareness of symptoms in the knee. A control group must represent the population in which the cases are taken from – this is fulfilled in this context, as the unicompartmental arthroplasty patients, with a mean age of 68, have had time for the PFOA to develop, proven by the case mean age of 60, with PFOA being recorded as early as the age of 29 years in some. The inclusion of this control group has also minimised the effects of other osteoarthritic-causing, therefore confounding, factors, such as increased exercise and obesity.

The adjusted OR calculations on previous patellar dislocation rates can be interpreted as a patient is approximately 3.2 times more likely to develop PFOA if they have had a patellar dislocation. On comparison of the ages of 1<sup>st</sup> dislocation, a difference of a median of 44 years suggests that patients who go on to develop PFOA experienced problems at a younger age than the controls. This would fit with the concept that the disease process begins in adolescence, far earlier than once thought.

Whilst reports of links between patellar dislocation and PFOA have been made in the literature, few are definitive. Previous research has focused on the evaluation of surgical techniques with data being collected after operations that may influence the progression of the disease [7, 8, 19]. These studies concluded that the surgical intervention itself is the primary predisposing factor for PFOA. Our study has demonstrated that although



previous surgery on the knee is significantly associated with the risk of developing PFOA (adjusted OR of 3.5), other factors such as patient reported previous dislocation (adjusted OR of 3.2), instability (adjusted OR of 3.5) or adolescent AKP (adjusted OR of 7.5) demonstrate similar or greater ORs.

In the case of patellar dislocation, the mechanism underlying this relationship may be due to the rapid movement of the patella out of the trochlear groove and over the edge of the lateral femoral condyle, then subsequent relocation. These movements lead to cartilage damage, and can initiate the pathological process that results in PFOA. Heywood noted this association, observing a 100% arthritis rate in those who had experienced dislocations for over 25 years [20]. A more likely explanation is that other anatomical variations, such as trochlea dysplasia and patella alta, may be associated with an increased risk of dislocation [21] and independent development of PFOA. Additionally, it has been argued that activity level of participants may act as a confounding factor to patellar problems and dislocation, with one study recording 70% of first presentations occurring following sport [22]. However, whilst often unmasking problems, sport would not cause these anatomical differences, providing further evidence to this underlying aetiology.

A major limitation of this study is the reduced reliability of data resulting from asking participants to recall their knee pain from adolescence. Whilst the unicompartamental control group attempts to take account of this, an increased chance of recall bias is present. Other limitations include its retrospective nature - it is impossible to determine how many individuals will go on to develop PFOA, and the end stage population in this report is far smaller than the population at-risk i.e. AKP is very common, and only a small proportion will actually go on to develop PFOA. A high loss to follow up ratio is also present in this cohort. Due to these factors, as well as the potentially imprecise appreciation of a small number of anatomical differences, larger prospective studies are required to further describe the relationships highlighted here.

## **5. Conclusions**

Based on the data presented, an association has been shown between adolescent anterior knee pain, a history of patella dislocation and the development of severe patellofemoral osteoarthritis. Further work is required in the area to account for the limitations aforementioned. This will help define these relationships at a more detailed level, and explain the aetiological mechanisms behind them, likely the discussed anatomical abnormalities. However, these results should bring into question the traditional belief that adolescent anterior knee pain is a benign pathology. These patients merit investigation, and we encourage clinical acknowledgement of the potential consequences when encountering patients suffering from both adolescent AKP and patellar dislocation.

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